

REMARKS

Reconsideration and continuing examination of the above-identified application is respectfully requested in view of the amendments above and the discussion that follows.

Withdrawal of the several previous rejections is noted with appreciation. Claims 1-46 are in the case and are before the Examiner. Claims 1, 11 and 25 have been amended as is discussed hereinbelow.

I. The Amendments

Claims 1, 11 and 25 have been amended to speed prosecution by cancelling the word "conservative".

New claim 47 has been added that combines claims 1 and 7 written together pursuant to the Examiner's helpful suggestion.

It is thus seen that no new matter has been added.

II. The Action

A. Rejection Under 35 USC §112, First Paragraph

All of the claims were newly rejected under the first paragraph of Section 112 as allegedly failing the description requirement and the enablement requirement. Although as noted in the prior Reply, it cannot be agreed that the previously provided amendments were not properly supported, each of independent claims 1, 11, and 25 has been amended to cancel the limitation that a substitution is conservative and speed prosecution. It is thus submitted that this basis for rejection is moot and should be withdrawn.

B. Rejections Under 35 USC §103

1. First Rejection

Claims 1-6, 8-14, 16-22, 30-42 and 46 have again been rejected as allegedly being obvious from the combined disclosures of Pumpens 1995, in view of Zlotnick (1997) and Zheng (1992). This rejection is again respectfully traversed.

The Action notes that the specification shows that C-terminally stabilized C48S/C107S chimera appeared to be entirely disulfide bonded at day zero, whereas its C48/C107 counterpart was not and did not reach the same level of cross-linking achieved by the C48S/C107S chimeras during the period of study, citing paragraph [0525], which should have been paragraph [0527] as was noted in the Reply. The Action correctly quoted the conclusion that "those results were intuitively unexpected and even more unexpected from the reading of Zheng in conjunction with Zlotnick."

The Action's response stated that those results were "found not persuasive because Zlotnick teaches that the C-terminal Cys can stabilize HBc $\Delta$ , and Zheng teaches that Cys<sup>48</sup> and Cys<sup>107</sup> are not essential for native core particle formation." Both statements are true. Both are taken out of context and are non sequiturs here.

Thus, both of the proteins [C48S/C107S and C48/C107] compared in the discussion of paragraph [0527] contained C-terminal Cys residues, making them "counterparts". As a consequence, Zlotnick's teaching about C-terminal Cys residues providing stabilization for his particle constructs says nothing about the observed difference in particle stability due to the presence or absence of internal Cys residues in otherwise identical constructs.

Similarly, the Zheng Abstract on page 9422 teaches about half-way through

[a]ll [proteins with and without Cys residues] assemble into essentially identical core particle structures. Therefore, disulfide bonds are not essential for core particle formation.

Thus, if "disulfide bonds are not essential for core particle formation", it is certainly true that the Cys residues of positions 48 and 107, being possible formers of disulfide bonds, are also "not essential" for particle formation.

These bases for rejection set up a simple syllogism that is contradictory in the present context. Zheng says that all disulfides do not matter. Cys<sup>48</sup> and Cys<sup>107</sup> can form disulfides, so Cys<sup>48</sup> and Cys<sup>107</sup> do not matter. Continuing that syllogism, the C-terminal Cys can also form a disulfide and therefore does not matter. That last part of the syllogism is, however, the lynch pin of the Action's argument concerning Zlotnick. Apparently, therefore, some disulfide bonds and some Cys residues do matter, and "not essential" means different things in different contexts. The Action thus poses a situation straight out of Lewis Carroll's Through the Looking Glass,

'When I use a word,' Humpty Dumpty said, in a rather scornful tone, 'it means just what I choose it to mean, neither more nor less.'

It is submitted that this type of Looking Glass definition can be avoided by further consulting the Zheng article. Following the above-quoted disclosure, Zheng teaches that there are no intrachain disulfides in his HBC particles,

and the Cys<sup>107</sup> is free (not oxidized) and buried. Two sentences further into the Abstract from the disclosure concerning what is "not essential", Zheng states

Cys<sup>61</sup> is always and Cys<sup>48</sup> is partly involved in interchain disulfide bonds with the identical residues of another monomer, whereas Cys<sup>183</sup> is always involved in a disulfide bond with the Cys<sup>183</sup> of another monomer.

Thus, contrary to the Action's argument, Cys<sup>48</sup> is involved in interchain disulfide bond formation and would therefore be thought by a worker of ordinary skill to provide some stability to the particle as a result of the presence of the disulfide bond. That being the case, it is again submitted that the results discussed in paragraph [0527] and shown in Fig. 4E-4H "were intuitively unexpected and even more unexpected from the reading of Zheng in conjunction with Zlotnick." Again, this basis for rejection should be withdrawn.

## 2. Second Rejection

Claims 1-6, 8-28 and 30-46 have also again been rejected as allegedly being obvious from the combined disclosures of Page et al. (WO 01/98333 A2) and Birkett (US 6,231,864) both in view of Zheng (1992). This rejection is respectfully traversed.

The Action again places its emphasis on the erroneous understanding of the Zheng teaching as to the functions of the Cys residues at HBC positions 48, 107 and 183, and cites to Paragraph 11 of the Action that was the basis for the previously discussed rejection. As noted above, the Zheng Abstract teaches

that Cys<sup>48</sup> participates in interchain disulfide bonding. The lower portion of the first full paragraph on the right column of page 9426 states that "Cys<sup>48</sup> may participate in disulfide bonding. When it does, it is between the same monomers as are linked by Cys<sup>61</sup>s." The last full paragraph on the right column of page 9426 begins with the sentence: "Cys<sup>48</sup> exists both as a disulfide and as free sulfhydryl in approximately equal amounts."

It should therefore be clear that Zheng teaches that Cys<sup>48</sup> provides interchain disulfide bonding. Interchain disulfide bonds are known by those who have successfully passed a first course in biochemistry to provide stability to protein structures. Here, the evidence shown in Figs. 4E-4H and that discussed in Paragraph [0527] show that a claimed HBc chimer lacking a Cys<sup>48</sup> residue that one would expect to provide stability was more stable than the otherwise identical chimer possessing that Cys<sup>48</sup> residue. That finding was and is unexpected and patentable. This basis for rejection should be withdrawn.

### III. Additional Information That May Be Material

In view of the holding in *McKesson Information Solutions, Inv. V. Bridge Medical, Inc.* (Fed. Cir. May 18, 2007; 06-1517), enclosed herewith are copies of Actions from an application relating to recombinant hepatitis B core particles and their use that might be deemed material to the prosecution of the present application. It is noted that the Examiner handling this application is also handling applications Serial No. 09/930,915; Serial No. 10/805,913 and Serial No. 10/806,006, as well as application Serial No. 10/787,734, so the Actions

from those applications are not being included herewith. The enclosed Actions are from application Serial No. 10/677,074, and are noted on enclosed Form PTO/SB/08B.

#### IV. Terminal Disclaimer

The Examiner's comments about obviousness-type double patenting and a terminal disclaimer are noted. However, inasmuch as no claims of any of the applications cited in the Action are noted to be allowable, let alone allowed, it is still believed to be premature to deal with a terminal disclaimer.

#### V. Summary

The independent claims have been amended to speed prosecution, and new claim 47 has been added pursuant to the Examiner's helpful suggestion. Each of the bases for rejection has been dealt with and overcome or otherwise made moot.

It is therefore believed that this application is in condition for allowance of all of the pending claims. An early notice to that effect is earnestly solicited.

No further fee or petition is believed to be necessary. However, should any further fee be needed, please charge our Deposit Account No. 23-0920, and deem this paper to be the required petition.

The Examiner is requested to phone the undersigned should any questions arise that can be dealt with over the phone to expedite this prosecution.

Respectfully submitted,

By

  
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Enclosures

Petition and Fee Extension of Time

Fee for filing Actions

Actions from other application, Form PTO/SB/08B

RCE and Fee

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